OM of: US-09-525-998A-11 to: A_Geneseq_1101:* out_format = pfs

Date: Apr 25, 2002 10:11 PM

About: Results were produced by the GenCore software, version 4.5,
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Command line parameters:
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Search information block:
Query: US-09-525-998A-11
Query length: 600
Database: A_Geneseq_1101:*
Database sequences: 522463
Database length: 74073290
Search time (sec): 140.140000

score_list:

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/SIDS2/gcgdata/geneseq/geneseqp/AA1998	DAT:	AAW89227	+	941.00	1636.69				2.1e-83	161 !
/SIDS2/gcgdata/geneseq/geneseqp/AA2000	DAT:	AAB37808	+	941.00	1636.69				2.1e-83	161 !
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seq_documentation_block:
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XX
AC   AAW89225;
XX
DT   04-MAR-1999 (first entry)
XX
DE   Tumour necrosis factor bp/osteoprotegerin construct INFBp 4.0.
XX
KW   Tumour necrosis factor receptor 1; TNFR 1; inhibitor; osteoprotegerin;
KW   OPG; chimeric fusion; dimerisation domain; autoimmune disease;
KW   inflammation; apoptosis.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
PN   WO9849305-A1.
XX
PD   05-NOV-1998.
XX
PF   29-APR-1998;   98WO-US08631.
XX
PR   01-MAY-1997;   97US-0850188.
XX
PA   (AMGE-) AMGEN INC.
XX
PI   Boyle WJ, Wooden S;
XX
DR   WPI; 1999-034001/03.
XX
PT   New chimeric osteoprotegerin polypeptides contain the
PT   osteoprotegerin dimerisation domain and a heterologous sequence,
PT   useful to treat TNF and TNFR mediated disorders
XX
PS   Example 2; Pat 6; 74pp; English.
XX
CC   The present invention describes a chimeric polypeptide (A1), comprising
CC   an osteoprotegerin (OPG) dimerisation domain fused to a heterologous
CC   amino acid sequence. Also described are: (2) a multimer polypeptide
CC   comprising covalently associated A1 monomers; (3) an isolated nucleic
CC   acid encoding A1; (4) an expression vector comprising the nucleic acid
CC   sequence; (5) a host cell transformed or transfected with the
CC   expression vector so that the nucleic acid is expressible. The products
CC   of the present invention are useful for treating a variety of disorders
CC   including those related to receptor binding. Compositions comprising
CC   TNFR1 or TNFR2 (TNFR), OPG and TNF receptor 1 (TNFR)/OPG chimeras
CC   are used to treat TNF and TNFR mediated disorders such as inflammation,
CC   autoimmune diseases and disorders treated by excessive apoptosis. The
CC   chimeras are also useful for detecting molecules which interact with
CC   TNFR1 or TNFR2 in a sample, as to identify potential new TNFR1 and
CC   TNFR2 ligands. The present sequence represents a DNA construct from
CC   the example of the present invention, i.e. a human TNFR1/OPG fusion
CC   protein.
XX
SQ   Sequence 211 AA;

alignment_scores:
Length: 211
Score: 1117.50
Gaps: 1
Percent Similarity: 94.787 Percent Identity: 94.787

alignment_block:
US-09-525-998A-11 x AAW89225 ..

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     51 GCTGTTGGTGGGAATATACCCCTCAGGGGTTATTGGA..... 87
        |||||||||||||||||||||||||||||||||||||
     17 uLeuLeuValGlyIleTyrProSerGlyValIleGlyLeuValProHisL 34

     88 ......      ...      GATAGTGTGTGTCCCCAAGGAAAATATATC 117
                            |||||||||||||||||||||||||||||
     34 euGlyAspArgGluLysArgAspSerValCysProGlnGlyLysTyrIle 50

    118 CACCCTCAAAATAATTCGATTTGCTGTACCAAGTGCCACAAAGGAACCTA 167
        ||||||||||||||||||||||||||||||||||||||||||||||||||
     51 HisProGlnAsnAsnSerIleCysCysThrLysCysHisLysGlyThrTy 67

    168 CTTGTACAATGACTGTCCAGGCCGGGGCAGGATACGGACTGCAGGGAGT 217
        ||||||||||||||||||||||||||||||||||||||||||||||||||
     67 rLeuTyrAsnAspCysProGlyProGlyGlnAspThrAspCysArgGluC 84

    218 CTGACAGCGGCTCCTTCACCGCTTCAGAAAACCACCTCAGACAGTGCCTC 267
        ||||||||||||||||||||||||||||||||||||||||||||||||||
     84 ysGluSerGlySerPheThrAlaSerGluAsnHisLeuArgHisCysLeu 100

    268 AGCTGCTCCAAATGCCGAAAGGAAATGGGTCAGGTGGAGATCTCTTCTTG 317
        ||||||||||||||||||||||||||||||||||||||||||||||||||
    101 SerCysSerLysCysArgLysGluMetGlyGlnValGluIleSerSerCy 117

    318 CACAGTGGACCGGGACACCGTGTGTGGCTGCAGGAAGAACCAGTACCGGC 367
        ||||||||||||||||||||||||||||||||||||||||||||||||||
    117 sThrValAspArgAspThrValCysGlyCysArgLysAsnGlnTyrArgH 134

    368 ATTATTGGAGTGAAAACCTTTCCAGTGCTCAATTGCAGCCTCTGCCTC 417
        ||||||||||||||||||||||||||||||||||||||||||||||||||
    134 isTyrTrpSerGluAsnLeuPheGlnCysPheAsnCysSerLeuCysLeu 150

    418 AATGGGACCGTGCACCTCTCCTGCCAGGAGAAACAGAACACCGTGTGCAC 467
        ||||||||||||||||||||||||||||||||||||||||||||||||||
    151 AsnGlyThrValHisLeuSerCysGlnGluLysGlnAsnThrValCysTh 167

    468 CTGCCATGCAGGTTTCTTTCTAAGAGAAAACGAGTGTGTCTCCTGTAGTA 517
        ||||||||||||||||||||||||||||||||||||||||||||||||||
    167 rCysHisAlaGlyPhePheLeuArgGluAsnGluCysValSerCysSerA 184

    518 ACTGTAAGAAAAGCCTGGAGTGCACGAAGTGTGTCCCTACCCCAGATTCAG 567
        ||||||||||||||||||||||||||||||||||||||||||||||||||
    184 snCysLysLysSerLeuGluCysThrLysLeuCysLeuProGlnIleGlu 200

    568 AATGTTAAGGGCACTGAGGACTCAGGCACCACA 600
        |||||||||||||||||||||||||||||||
    201 AsnValLysGlyThrGluAspSerGlyThrThr 211

seq name  /SIDS2/gcgdata/geneseq/geneseqp/AA2001.DAT:AAB66979

seq_documentation_block:
ID   AAB66979 standard; Protein; 280 AA.
XX
AC   AAB66979;
XX
DT   19-APR-2001  (first entry)
XX
DE   Tnfrl protein.
XX
KW   Bone loss; osteoprotegerin; OPG; rheumatoid arthritis; hyperalgesia;
KW   multiple sclerosis; osteoporosis; osteomyelitis; asthma; inflammation;
KW   systemic lupus erythematosus; graft-versus-host disease; septic shock;
KW   acute pancreatitis, Alzheimer's disease, anorexia; atherosclerosis; pain;
KW   coronary condition, myocardial infarction; cancer, diabetes, psoriasis,
KW   endometriosis, fever; glomerulonephritis; inflammatory bowel disease;
KW   ischaemia; Parkinson's disease.
XX
OS   Unidentified.
XX
PN   WO200103719-A2.
XX
PD   18-JAN-2001.
XX
PF   07-JUL-2000; 2000WO-US18667.
XX
PR   09-JUL-1999;   99US-0350670.
PR   09-DEC-1999;   99US-0457647.
XX
PA   (AMGE-) AMGEN INC.
XX
PI   Boyle WJ,  Lacey DL,  Calzone FJ,  Chang M,  Senaldi G;
XX
DR   WPI; 2001-103031/11.
XX
PT   Treating conditions leading to bone loss such as rheumatoid arthritis,
PT   multiple sclerosis and asthma, comprises administering an
PT   osteoprotegerin protein in conjunction with e.g. inhibitors of
PT   interleukin and tumor necrosis factor alpha  -
XX
PS   Disclosure; Fig 2; 316pp; English.
XX
CC   The present invention relates to a method for treating conditions leading
CC   to bone loss. The method comprises administering a purified and isolated
CC   osteoprotegerin (OPG) protein (AAF57836-AAF57838 and AAB66974-AAB66976)
CC   in conjunction with other substances such as tumour necrosis factor-alpha
CC   (TNF-alpha) inhibitors, interleukin (IL)-6, -8 and -18 inhibitors, ICE
CC   modulators, fibroblast growth factor (FGF)1-10 modulators and/or platelet
CC   activating factor (PAF) antagonists. The method is useful for treating
CC   conditions leading to bone loss such as rheumatoid arthritis, multiple
CC   sclerosis, osteoporosis, osteomyelitis and asthma. The method is also
CC   useful for treating inflammation, systemic lupus erythematosus (SLE) and
CC   graft-versus-host disease (GvHD). Other diseases that can be treated
CC   include acute pancreatitis, Alzheimer's disease, anorexia,
CC   atherosclerosis, coronary conditions (e.g. myocardial infarction),
CC   cancer, diabetes, endometriosis, fever, glomerulonephritis, hyperalgesia,
CC   inflammatory bowel disease, ischaemia, pain, Parkinson's disease,
CC   psoriasis and septic shock. The present sequence was used in a sequence
CC   homology comparison.
XX
SQ   Sequence   280 AA;


alignment_scores:
           Quality: 1117.50              Length:    211
             Ratio:  5.588                Gaps:      1
 Percent Similarity:  94.787   Percent Identity: 94.787

alignment_block:
 US-09-525-998A-11 x AAB66979   ..

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      51 GCTGTTGGTGGGAATATACCCCTCAGGGGTTATTGGA..... 87
         |||||||||||||||||||||||||||||||||||||
      17 uLeuLeuValGlyIleTyrProSerGlyValIleGlyLeuValProHisL 34

      88 ..      ...      GATAGTGTGTGTCCCCAAGGAAAATATATC 117
                          |||||||||||||||||||||||||||||
      34 euGlyAspArgGluLysArgAspSerValCysProGlnGlyLysTyrIle 50

     118 CACCCTCAAAATAATTCGATTTGCTGTACCAAGTGCCACAAAGGAACCTA 167
         ||||||||||||||||||||||||||||||||||||||||||||||||||
      51 HisProGlnAsnAsnSerIleCysCysThrLysCysHisLysGlyThrTy 67

     168 CTTGTACAATGACTGTCCAGGCCGGGGCAGGATACGGACTGCAGGGAGT 217
         ||||||||||||||||||||||||||||||||||||||||||||||||||
```

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 67 rLeuTyrAsnAspCysProGl,ProGlyGluAspThrAspCysArgGluC 84

218 CTGAGAGCGGCTCCTTCACCCTTCAGAAAACCACCTCAGACACTGCCTC 267
    ||||||||||||||||||||||||||||||||||||||||||||||||||
 84 ysGluSerGlySerPheThrAlaSerGluAsnHisLeuArgHisCysLeu 100

268 AGCTGCTCCAAATGCCGAAAGGAAATGGGTCAGGTGGAGATCTCTTCTTG 317
    ||||||||||||||||||||||||||||||||||||||||||||||||||
101 SerCysSerLysCysArgLysGluMetGlyGlnValGluIleSerSerCy 117

318 CACAGTGGACCGGCACACCGTGTGTGGCTGCAGGAAGAACCAGTACCGGC 367
    ||||||||||||||||||||||||||||||||||||||||||||||||||
117 sThrValAspArgAspThrValCysGlyCysArgLysAsnGlnTyrArgH 134

368 ATTATTGGAGTGAAAACCTTTTCCAGTGCTTCAATTGCAGCCCTCTGCCTC 417
    ||||||||||||||||||||||||||||||||||||||||||||||||||
134 isTyrTrpSerGluAsnLeuPheGlnCysPheAsnCysSerLeuCysLeu 150

418 AATGGGACCGTGCACCTCTCCTGCCAGGAGAAACAGAACACCGTGTGCAC 467
    ||||||||||||||||||||||||||||||||||||||||||||||||||
151 AsnGlyThrValHisLeuSerCysGlnGluLysGlnAsnThrValCysTh 167

468 CTGCCATGCAGGTTTCTTTCTAAGAGAAAACGAGTGTGTCTCCTGTAGTA 517
    ||||||||||||||||||||||||||||||||||||||||||||||||||
167 rCysHisAlaGlyPhePheLeuArgGluAsnGluCysValSerCysSerA 184

518 ACTGTAAGAAAAGCCTGCAGTGCCACGAACTTGTGCCTACCCCAGATTCAG 567
    ||||||||||||||||||||||||||||||||||||||||||||||||||
184 snCysLysLysSerLeuGlnCysThrLysGluCysLeuProGlnIleGlu 200

568 AATGTTAAGGGCACTGAGGACTCAGGCACCACA 600
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seq_documentation_block:
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XX
AC   AAW89229;
XX
DT   04-MAR-1999  (first entry)
XX
DE   Tumour necrosis factor bp/osteoprotegerin construct TNFbp/304.
XX
KW   Tumour necrosis factor receptor 1; TNFR-1; inhibitor; osteoprotegerin;
KW   OPG; chimeric; fusion; dimerisation domain; autoimmune disease;
KW   inflammation; apoptosis.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
PN   WO9849305-A1.
XX
PD   05-NOV-1998.
XX
PF   29-APR-1998;   98WO-US08631.
XX
PR   01-MAY-1997;   97US-0850188.
XX
PA   (AMGE-) AMGEN INC.
XX
PI   Boyle WJ,  Wooden S;
XX
DR   WPI; 1999-034661/03
XX
PT   New chimeric osteoprotegerin polypeptides - contain the
PT   osteoprotegerin dimerisation domain and a heterologous sequence,
PT   useful to treat TNF and TNFR-mediated disorders
XX
PS   Example 1; Fig 4; 92pp; English.
XX
CC   The present invention describes a chimeric polypeptide (A1), comprising
CC   an osteoprotegerin (OPG) dimerisation domain fused to a heterologous
CC   amino acid sequence. Also described are: (1) a multimer polypeptide
CC   comprising covalently associated A1 monomers; (2) an isolated nucleic
CC   acid encoding A1; (3) an expression vector comprising the nucleic acid
CC   sequence; and (4) a host cell transformed or transfected with the
CC   expression vector so that the nucleic acid is expressible. The products
CC   from the present invention are useful to treat a variety of disorders
CC   including those related to receptor binding. Compositions comprising
CC   tumour necrosis factor (TNF)/OPG and TNF receptor (TNFR)/OPG chimeras
CC   are used to treat TNF and TNFR mediated disorders such as inflammation,
CC   autoimmune diseases and disorders related to excessive apoptosis. The
CC   chimeras are also useful for detecting molecules which interact with
CC   fused heterologous sequences to identify potential new receptors and
CC   ligands. The present sequence represents a TNFbp/OPG construct from
CC   the example of the present invention for creating TNFbp/OPG fusion
CC   proteins.
XX
SQ   Sequence   311 AA;


alignment_scores:
            Quality: 1117.50              Length:    211
              Ratio:  5.588                Gaps:      1
 Percent Similarity:  94.787   Percent Identity: 94.787

alignment_block:
US-09-525-998A-11 x AAW89229   ..

 Align seq 1/1  to.. AAW89229  from. 1  to... 311

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       1 MetGlyLeuSerThrValProAspLeuLeuLeuProLeuValLeuLeuGl 17

      51 GCTGTTGGTGGAAIAIACGCCTCAGGGTTTATTGGA.............. 87
         ||||||||||:|||||||||||||||||||||||||
      17 aLeuLeuValGlyIleTyrProSerGlyValIleGlyLeuValProHisL 34

      88 ....................CATAGTGTGTGTCCCCAAGGAAAAATATATC 117
                             |||||||||||||| ||||||||||||||
      34 euGlyAspArgGluLysArgAspSerValCysProGlnGlyLysTyrIle 50

     118 CACCCTCAAAATAATTCGATTTGCTGTACCAAGTGCCACAAAGGAACCTA 167
         |||||||||||||||||||||||||||||||| ||||||||||||||||
      51 HisProGlnAsnAsnSerIleCysCysThrLysCysHisLysGlyThrTy 67

     168 CTCCACAACAGCAGTGTCCAGCCCCGGGGCAGCATATCCACTCCAGCCACT 217
         ||||||||||||||||||||||||||||||||||||||||||||||||||
      67 rLeuTyrAsnAspCysProGlyProGlyGlnAspThrAspCysArgGluC 84

     218 CTGAGAGCGGCTCCTTCACCGTTCAGAAAACCACCTCAGACACTGCCTC 267
         ||||||||||||||||||||||||||||||||||||||||||||||||||
      84 ysGluSerGlySerPheThrAlaSerGluAsnHisLeuArgHisCysLeu 100

     268 AGCTGCTCCAAATGCCGAAAGGAAATGGGTCAGGTGGAGATCTCTTCTTG 317
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     101 SerCysSerLysCysArgLysGluMetGlyGlnValGluIleSerSerCy 117

     318 CACAGTGGACCGGCACACCGTGTGTGGCTGCAGGAAGAACCAGTACCGGC 367
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     117 sThrValAspArgAspThrValCysGlyCysArgLysAsnGlnTyrArgH 134

     368 ATTATTGGAGTGAAAACCTTTTCCAGTGCTTCAATTGCAGCCCTCTGCCTC 417
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     134 isTyrTrpSerGluAsnLeuPheGlnCysPheAsnCysSerLeuCysLeu 150

     418 AATGGGACCGTGCACCTCTCCTGCCAGGAGAAACAGAACACCGTGTGCAC 467
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     151 AsnGlyThrValHisLeuSerCysGlnGluLysGlnAsnThrValCysTh 167

     468 CTGCCATGCAGGTTTCTTTCTAAGAGAAAACGAGTGTGTCTCCTGTAGTA 517
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     167 rCysHisAlaGlyPhePheLeuArgGluAsnGluCysValSerCysSerA 184
```

```
     518 ACTGTAAGAAAAGCCTGGAGTGCACGAAGTTGTGCCTACCCCAGATTGAG 567
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     184 snCysLysLysSerLeuGluCysThrLysLeuCysLeuProGlnIleGlu 200

     568 AATGTTAAGGGCACTCAGGACTCAGGCACCACA 600
         ||||||||||||||||||||||||||||||||
     201 AsnValLysGlyThrGluAspSerGlyThrThr 211

seq_name: /SIDS2/gcgdata/geneseq/geneseqp/AA1990 DAT AAW89228

seq_documentation_block:
ID   AAW89228 standard; Protein; 366 AA.
XX
AC   AAW89228;
XX
DT   04-MAR-1999  (first entry)
XX
DE   Tumour necrosis factor bp/osteoprotegerin construct TNFbp/248.
XX
KW   Tumour necrosis factor receptor 1; TNFR-1; inhibitor; osteoprotegerin;
KW   OPG; chimeric; fusion; dimerisation domain; autoimmune disease;
KW   inflammation; apoptosis.
XX
OS   Homo sapiens.
OS   Synthetic
XX
PN   WO9849305-A1.
XX
PD   05-NOV-1998.
XX
PF   29-APR-1998;   98WO-US08631.
XX
PR   01-MAY-1997;   97US-0850188
XX
PA   (AMGE-) AMGEN INC.
XX
PI   Boyle WJ,  Wooden S;
XX
DR   WPI; 1999-034661/03.
XX
PT   New chimeric osteoprotegerin polypeptides - contain the
PT   osteoprotegerin dimerisation domain and a heterologous sequence,
PT   useful to treat TNF and TNFR-mediated disorders
XX
PS   Example 1; Fig 4; 92pp; English.
XX
CC   The present invention describes a chimeric polypeptide (A1), comprising
CC   an osteoprotegerin (OPG) dimerisation domain fused to a heterologous
CC   amino acid sequence. Also described are: (1) a multimer polypeptide
CC   comprising covalently associated A1 monomers; (2) an isolated nucleic
CC   acid encoding A1; (3) an expression vector comprising the nucleic acid
CC   sequence; and (4) a host cell transformed or transfected with the
CC   expression vector so that the nucleic acid is expressible. The products
CC   from the present invention are useful to treat a variety of disorders
CC   including those related to receptor binding. Compositions comprising
CC   tumour necrosis factor (TNF)/OPG and TNF receptor (TNFR)/OPG chimeras
CC   are used to treat TNF and TNFR-mediated disorders such as inflammation,
CC   autoimmune diseases and disorders related to excessive apoptosis. The
CC   chimeras are also useful for detecting molecules which interact with
CC   fused heterologous sequences to identify potential new receptors and
CC   ligands. The present sequence represents a TNFbp/OPG construct from
CC   the example of the present invention for creating TNFbp/OPG fusion
CC   proteins.
XX
SQ   Sequence   366 AA;


alignment_scores:
            Quality: 1117.50              Length:    211
              Ratio:  5.588                Gaps:      1
 Percent Similarity:  94.787   Percent Identity: 94.787
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alignment_block:
 US-09-525-998A-11 x AAW89228   ..

 Align seq 1/1  to: AAW89228  from: 1  to: 366

       1 ATGGGCCTCTCCACCGTGCCTGACCTGCTGCTGCCAGTGGTGCTCCTGGA 50
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       1 MetGlyLeuSerThrValProAspLeuLeuLeuProLeuValLeuLeuGl 17

      51 GCTGTTGGTGGGAATATACCCTCAGGGTTATTGGA                87
         ||||||||||||||||||||||||||||||||||||
      17 uLeuLeuValGlyIleTyrProSerGlyValIleGlyLeuValProHisL 34

      88 ..........          GATAGTGTGTGTCCCCAAGGAAAATATATC 117
                             ||||||||||||||||||||||||||||||
      34 euGlyAspArgGluLysArgAspSerValCysProGlnGlyLysTyrIle 50

     118 CACCCTCAAAATAATTCGATTTGCTGTACCAAGTGCCACAAAGGAACCTA 167
         ||||||||||||||||||||||||||||||||||||||||||||||||||
      51 HisProGlnAsnAsnSerIleCysCysThrLysCysHisLysGlyThrTy 67

     168 CTTGTACAATGACTGTCCAGGCCCGGGCAGGATACGGACTGCAGGAGT 217
         ||||||||||||||||||||||||||||||||||||||||||||||||||
      67 rLeuTyrAsnAspCysProGlyProGlyGlnAspThrAspCysArgGluC 84

     218 CTGAGAGCGGCTCCTTCACCGCTTCAGAAAACACACCTCACACACTGCCTC 267
         ||||||||||||||||||||||||||||||||||||||||||||||||||
      84 ysGluSerGlySerPheThrAlaSerGluAsnHisLeuArgHisCysLeu 100

     268 AGCTGCTCCAAATGCCGAAAGGAAATGGGTCAGCTGGAGATCTCTTCTTG 317
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     101 SerCysSerLysCysArgLysGluMetGlyGlnValGluIleSerSerCy 117

     318 CACAGTGGACCGGGACACCGTGTGTGGCTGCAGGAAGAACCAGTACCGGC 367
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     117 sThrValAspArgAspThrValCysGlyCysArgLysAsnGlnTyrArgH 134

     368 ATTATTGGAGTGAAAACCTTTTCCAGTGCTTCAATTGCAGCCTCTGCCTC 417
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     134 isTyrTrpSerGluAsnLeuPheGlnCysPheAsnCysSerLeuCysLeu 150

     418 AATGGGACCGTGCACCTCTCCTGCCAGGAGAAACAGAACACCGTGTGCAC 467
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     151 AsnGlyThrValHisLeuSerCysGlnGluLysGlnAsnThrValCysTh 167

     468 CTGCATGCAGGTTTCTTTCTAAGAGAAAACGAGTGTGTCCCTGTAGTA 517
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     167 rCysHisAlaGlyPhePheLeuArgGluAsnGluCysValSerCysSerA 184

     518 ACTGTAAGAAAAGCCTGGAGTGCACGAAGTTGTGCCTACCCCAGATTGAG 567
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     184 snCysLysLysSerLeuGluCysThrLysLeuCysLeuProGlnIleGlu 200

     568 AATGTTAAGGGCACTCAGGACTCAGGCACCACA 600
         ||||||||||||||||||||||||||||||||
     201 AsnValLysGlyThrGluAspSerGlyThrThr 211

seq_name: /SIDS2/gcgdata/geneseq/geneseqp/AA1990 DAT:AAR07449

seq_documentation_block:
ID   AAR07449 standard; protein; 371 AA.
XX
AC   AAR07449;
XX
DT   29-JAN-1991  (first entry)
XX
DE   Tumour Necrosis Factor-Binding Protein from pTNF-BP15 cDNA.
XX
KW   Tumour necrosis factor binding protein; TNF-BP; TNF-receptor;
KW   pTNF-BP15; infectious disease; parasitic disease; cachexia;
KW   autoimmune disease; shock.
XX
OS   Homo sapiens.
```

```
XX
PN   EP393438-A.
XX
PD   24-OCT-1990.
XX
PF   06-APR-1990;   90EP-0106624.
XX
PR   21-JUN-1989;   89DE-3920282.
PR   21-APR-1989;   89DE-3913101.
XX
PA   (BOEH ) BOEHRINGER INGELHEIMINT.
XX
PI   Hauptmann R,  Himmler A,  Maurer-Fogy I,  Stratowa C;
XX
DR   WPI; 1990-321987/43.
DR   N-PSDB; AAQ06282.
XX
PT   DNA encoding TNF binding protein and TNF- receptor - used in
PT   tumour treatment and to understand mechanismsm to TNF action
XX
PS   Disclosure; Fig 1(1-3); 51pp; German.
XX
CC   Clone pTNF-BP15 was used to contruct pADTNF-BP, for transfection of
CC   e.g. COS7 cells.  The expressed proteins are useful
CC   prophylactically and therapeutically to control disorders which
CC   involve the damaging effects of TNF-alpha or -beta (e.g. infectious or
CC   parasitic diseases, shock, cachexia, autoimmune diseases, adult
CC   respiratory distress syndrome etc., or side effects of treatment with
CC   TNG-alpha).  They can also be used as diagnostic reagents for
CC   assaying TNF and in study of TNF-receptor interactions.
CC   See also AAQ06282-Q06285.
XX
SQ   Sequence   371 AA;


alignment_scores:
            Quality: 1117.50              Length:    211
              Ratio:  5.588                Gaps:      1
 Percent Similarity:  94.787   Percent Identity:  94.787

alignment_block:
 US-09-525-998A-11 x AAR07449   ..

 Align seq 1/1  to: AAR07449  from: 1  to: 371

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         ||||||||||||||||||||||||||||||||||||||||||||||||||
       1 MetGlyLeuSerThrValProAspLeuLeuLeuProLeuValLeuLeuGl 17

      51 GCICTTGGTGGGAATATACCCCTCAGGGGTTATTGGA..............  87
         ||||||||||||||||||||||||||||||||||||
      17 uLeuLeuValGlyIleTyrProSerGlyValIleGlyLeuValProHisL 34

      88 ........    .  .  .  CATAGTGTGTGTCCCCAAGCAAAATATATC 117
                              |||||||||||||||||||||||||||||||
      34 euGlyAspArgGluLysArgAspSerValCysProGlnGlyLysTyrIle 50

     118 CACCCTCAAAATAATTGGATTTGCTGTACCAAGTGCCACAAAGGAACCTA 167
         ||||||||||||||||||||||||||||||||||||||||||||||||||
      51 HisProGlnAsnAsnSerIleCysCysThrLysCysHisLysGlyThrTy 67

     168 CTTGTACAATGACTGTCCAGGCCCGGGCAGCATACGCAGTGGAGGAGT 217
         ||||||||||||||||||||||||||||||||||||||||||||||||||
      67 rLeuTyrAsnAspCysProGlyProGlyGlnAspThrAspCysArgGluC 84

     218 CTCACAGCCCCTCCTCACCCCTGCAGAAACCACCTCACACAGTGCCTTC 267
         ||||||||||||||||||||||||||||||||||||||||||||||||||
      84 ysGluSerGlySerPheThrAlaSerGluAsnHisLeuArgHisCysLeu 100

     268 AGCTGTTCCAAATGCCGAAAGGAAATGGGTCAGGTGGAGATCTCTTCTTG 317
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     101 SerCysSerLysCysArgLysGluMetGlyGlnValGluIleSerSerCy 117

     318 CACACTGGACCGGCACACCGTGTGTGGCTGCAGGAAGAACCAGTACCGGC 367
         |||||||||||||||||||||||||||||||||||||||||||||||||
     117 sThrValAspArgAspThrValCysGlyCysArgLysAsnGlnTyrArgH 134

     368 ATTATTGGAGTGAAAACCTTTTCCAGTGCTTCAATTGCAGCCTCTGCCTC 417
         |||||||||||| ||||||||||||||||||||||||||||||||||||
     134 isTyrIrpSerGluAsnLeuPheGlnCysPheAsnCysSerLeuCysLeu 150

     418 AATGGGACCGTGCACCTCTCCTGCCAGGAGAAACAGAACACCGTGTGCAC 467
         |||||||||||||||||||||||||||||||||||||||||||||||||
     151 AsnGlyThrValHisLeuSerCysGlnGluLysGlnAsnThrValCysTh 167

     468 CTGCCATGCAGGTTTCTTTCTAACAGAAAACGAGTGTGTCTGCAATGCTA 517
         |||||||||||| ||| |||||||||||||||||||||||||||||||||
     167 rCysHisAlaGlyPhePheLeuArgAsnGluLysValSerCysSerA 184

     518 ACTGTAAGAAAAGCCTGGAGTGCACGAAGTTGTGCCTACCCCAGATTGAG 567
         |||||||||||| ||||||||||||||||||||||||||||||||||||
     184 snCysLysLysSerLeuGluCysThrLysLeuCysLeuProGlnIleGlu 200

     568 AATGTTAAGGGCACTGAGGACTCAGGCACCACA 600
         |||||||||||| ||||||||||||||||||||
     201 AsnValLysGlyThrGluAspSerGlyThrThr 211

Search Summary  Database: US92_genbank_AA.seq;*;GenPept_AA.seq;*;AAW89227

seq_documentation_block:
ID   AAW89227 standard; Protein; 397 AA.
XX
AC   AAW89227;
XX
DT   04-MAR-1999  (first entry)
XX
DE   Tumour necrosis factor receptor 1/osteoprotegerin fusion protein TNFR1/217.
XX
KW   Tumour necrosis factor receptor 1; TNFR-1; inhibitor; osteoprotegerin;
KW   OPG; chimeric; fusion; dimerisation domain; autoimmune disease;
KW   inflammation; apoptosis.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
PN   WO9849305-A1.
XX
PD   05-NOV-1998.
XX
PF   29-APR-1998;   98WO-US08631.
XX
PR   01-MAY-1997;   97US-0850188.
XX
PA   (AMGE-) AMGEN INC.
XX
PI   Boyle WJ,  Wooden S;
XX
DR   WPI; 1999-034661/03.
XX
PT   New chimeric osteoprotegerin polypeptides - contain the
PT   osteoprotegerin dimerisation domain and a heterologous sequence,
PT   useful to treat TNF and TNFR-mediated disorders
XX
PS   Example 1; Fig 4; 92pp; English.
XX
CC   The present invention describes a chimeric polypeptide (A1), comprising
CC   an osteoprotegerin (OPG) dimerisation domain fused to a heterologous
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CC   sequence; and (4) a host cell transformed or transfected with the
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CC   from the present invention are useful to treat a variety of disorders
CC   including those related to receptor binding. Compositions comprising
CC   tumour necrosis factor (TNF), OPG and TNF receptor (TNFR); OPG chimeras
CC   are used to treat TNF and TNFR-mediated disorders such as inflammation,
```

```
CC   autoimmune diseases and disorders related to excessive apoptosis. The
CC   chimeras are also useful for detecting molecules which interact with
CC   fused heterologous sequences to identify potential new receptors and
CC   ligands. The present sequence represents a TNFbp/OPG construct from
CC   the example of the present invention for creating TNFbp/OPG fusion
CC   proteins.
XX
SQ   Sequence   397 AA;


alignment_scores:
            Quality: 1117.50              Length:    211
              Ratio:  5.588                Gaps:      1
 Percent Similarity:  94.787   Percent Identity: 94.787

alignment_block:
 US-09-525-998A-11 x AAW89227   ..

 Align seq 1/1  to: AAW89227  from: 1  to: 397

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       1 MetGlyLeuSerThrValProAspLeuLeuLeuProLeuValLeuLeuGl 17

      51 GCTGTTGGTGGGAAATATACCCCTCAGGGCTTATTGCA           ... 87
         ||||||||||||||||||||||||||||||||||||
      17 LeuLeuValGlyIleTyrProSerGlyValIleGlyLeuValProHisL 34

      88 ...                   GATAGTGTGTGTCCCCAAGGAAAAATATATC 117
                                 |||||||||||||||||||||||||||||
      34 euGlyAspArgGluLysArgAspSerValCysProGlnGlyLysTyrIle 50

     118 CACCCTCAAAATAATTCGATTTGCTGTACCAAGTGCCACAAAGGAACCTA 167
         ||||||||||||||||||||||||||||||||||||||||||||||||||
      51 HisProGlnAsnAsnSerIleCysCysThrLysCysHisLysGlyThrTy 67

     168 CTTGTACAATGACTGTCCAGGCCCGGGCCAGGATACCCACTCCACCCACT 217
         ||||||||||||||||||||||||||||||||||||||||||||||||||
      67 rLeuTyrAsnAspCysProGlyProGlyGlnAspThrAspCysArgGluC 84

     218 GTGAGAGCGGCTCCTTCACCGCTTCAAAAACACACGTCAGACACTGCTCT 267
         ||||||||||||||||||||||||||||||||||||||||||||||||||
      84 ysGluSerGlySerPheThrAlaSerGluAsnHisLeuArgHisCysLeu 100

     268 AGCTGCTCCAAATGCCGAAAGGAAATGGGTCAGGTGGAGATCTCTTCTTG 317
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     101 SerCysSerLysCysArgLysGluMetGlyGlnValGluIleSerSerCy 117

     318 CACAGTGGACCGGGACACCGTGTGTGGCTGCACCAAGAACCAGTACCGGC 367
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     117 sThrValAspArgAspThrValCysGlyCysArgLysAsnGlnTyrArgH 134

     368 ATTATTGGAGTGAAAACCTTTTCCAGTGCTTCAATTGCAGCCTCTGCCTC 417
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     134 isTyrTrpSerGluAsnLeuPheGlnCysPheAsnCysSerLeuCysLeu 150

     418 AATGGGACCGTGCACCTCTCCTGCCAGGAGAAACAGAACACCGTGTGCAC 467
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     151 AsnGlyThrValHisLeuSerCysGlnGluLysGlnAsnThrValCysTh 167

     468 CTGCCATGCAGGTTTCTTTCTAAGAGAAAACGAGTGTGTCTCCTGTAGTA 517
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     167 rCysHisAlaGlyPhePheLeuArgGluAsnGluCysValSerCysSerA 184

     518 ACTGTAAGAAAAGCCTGGAGTGCAAGAAGTTGTGCCTACCCCAGATTGAG 567
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     184 snCysLysLysSerLeuGluCysThrLysLeuCysLeuProGlnIleGlu 200

     568 AATGTTAAGGGCAGTGAGGACTCAGGCACCACA 600
         |||||||||||||||||||||||||||||||
     201 AsnValLysGlyThrGluAspSerGlyThrThr 211

seq_name: /S1AS2/acgdata/genseq2/genseqB/AAIDOC1AI_AAW89226
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seq_documentation_block:
ID   AAW89226 standard; Protein; 417 AA.
XX
AC   AAW89226;
XX
DT   04-MAR-1999  (first entry)
XX
DE   Tumour necrosis factor bp/osteoprotegerin construct TNFbp/196.
XX
KW   Tumour necrosis factor receptor 1; TNFR-1; inhibitor; osteoprotegerin;
KW   OPG; chimeric; fusion; dimerisation domain; autoimmune disease;
KW   inflammation; apoptosis.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
PN   WO9849305-A1.
XX
PD   05-NOV-1998.
XX
PF   29-APR-1998;   98WO-US08631.
XX
PR   01-MAY-1997;   97US-0850188.
XX
PA   (AMGE-) AMGEN INC.
XX
PI   Boyle WJ,  Wooden S;
XX
DR   WPI; 1999-034661/03.
XX
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PT   osteoprotegerin dimerisation domain and a heterologous sequence,
PT   useful to treat TNF and TNFR-mediated disorders
XX
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XX
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CC   amino acid sequence. Also described are: (1) a multimer polypeptide
CC   comprising covalently associated A1 monomers; (2) an isolated nucleic
CC   acid encoding A1; (3) an expression vector comprising the nucleic acid
CC   sequence; and (4) a host cell transformed or transfected with the
CC   expression vector so that the nucleic acid is expressible. The products
CC   from the present invention are useful to treat a variety of disorders
CC   including those related to receptor binding. Compositions comprising
CC   tumour necrosis factor (TNF)/OPG and TNF receptor (TNFR)/OPG chimeras
CC   are used to treat TNF and TNFR-mediated disorders such as inflammation,
CC   autoimmune diseases and disorders related to excessive apoptosis. The
CC   chimeras are also useful for detecting molecules which interact with
CC   fused heterologous sequences to identify potential new receptors and
CC   ligands. The present sequence represents a TNFbp/OPG construct from
CC   the example of the present invention for creating TNFbp/OPG fusion
CC   proteins.
XX
SQ   Sequence   417 AA;


alignment_scores:
            Quality: 1117.50              Length:    211
              Ratio:  5.588                Gaps:      1
 Percent Similarity:  94.787   Percent Identity: 94.787

alignment_block:
 US-09-525-998A-11 x AAW89226   ..

 Align seq 1/1  to: AAW89226  from: 1  to: 417

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       1 MetGlyLeuSerThrValProAspLeuLeuLeuProLeuValLeuLeuGl 17

      51 GCTGTTGGTGGGAAATATACCCCTCAGGGCTTATTGCA..... 87
```

```
      17 uLeuLeuValGlyIleTyrProSerGlyValIleGlyLeuValProHisL 34

      88 .....GATAGTGTGTGTCCCCAAGGAAAATATATC 117
                 ||||||||||||||||||||||||||||||
      34 euGlyAspArgGluLysArgAspSerValCysProGlnGlyLysTyrIle 50

     118 CACCCTCAAAATAATTCGATTGCTGTACCAAGTGCCACAAAGGAACCTA 167
         |||||||||||||||:||||||||||||||||||||||||||||||||
      51 HisProGlnAsnAsnSerIleCysCysThrLysCysHisLysGlyThrTy 67

     168 CTTGTACAATGACTGTCCAGGCCCGGGGCAGGATACCGACTGCAGGGAGT 217
         ||||||||||||||||||||||||||||||||||||||||||||||||||
      67 rLeuTyrAsnAspCysProGlyProGlyGlnAspThrAspCysArgGluC 84

     218 CTGAGAGCGGCTCCTTCACCGCTTCAGAAAACCACCTCAGACACTGCCTC 267
         ||||||||||||||||||||||||||||||||||||||||||||||||||
      84 ysGluSerGlySerPheThrAlaSerGluAsnHisLeuArgHisCysLeu 100

     268 AGCTGCTCCAAATGCCGAAAGGAAAAGGGTCAGGTGGAGATCTCTTCTTG 317
         ||||||||||||||:||||||||||||||||||||||||||||||||||
     101 SerCysSerLysCysArgLysGluMetGlyGlnValGluIleSerSerCy 117

     318 CACAGTGGACCGGGACACCGTGTGTGGCTGCAGGAAGAACCAGTACCGGC 367
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     117 sThrValAspArgAspThrValCysGlyCysArgLysAsnGlnTyrArgH 134

     368 ATTATTGGAGTGAAAACCTTTTCCAGTGCTTCAATTGCAGCCTCTGCCTC 417
         ||||||||||||||:||||||||||||||||||||||||||||||||||
     134 isTyrTrpSerGluAsnLeuPheGlnCysPheAsnCysSerLeuCysLeu 150

     418 AATGGGACCGTGCACCTCTCCTGCCAGGAGAAACAGAACACCGTGTGCAC 467
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     151 AsnGlyThrValHisLeuSerCysGlnGluLysGlnAsnThrValCysTh 167

     468 CTGCCATGCAGGTTTCTTTCTAAGAGAAAACGAGTGTGTCTCCTGTAGTA 517
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     167 rCysHisAlaGlyPhePheLeuArgGluAsnGluCysValSerCysSerA 184

     518 ACTGTAAGAAAAGCCTGGAGTGCATGAAGTTGTGCCTACCCCAGATTGAG 567
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     184 snCysLysLysSerLeuGluCysMetLysLeuCysLeuProGlnIleGlu 200

     568 AATGTTAAGGGCACTGAGGACTCAGGCACCACA 600
         ||||||||||||||||||||||||||||||||
     201 AsnValLysGlyThrGluAspSerGlyThrThr 211

seq_name: STN1/pogdata/pctseq/pctseqpg/AAW89224.pep.1A; AAW89224

seq_documentation_block:
ID   AAW89224 standard; Protein; 420 AA.
XX
AC   AAW89224;
XX
DT   04-MAR-1999  (first entry)
XX
DE   Tumour necrosis factor bp/osteoprotegerin construct TNFbp/OPG.
XX
KW   Tumour necrosis factor receptor 1; TNFR-1; inhibitor; osteoprotegerin;
KW   OPG; chimeric, fusion, dimerisation domain, autoimmune disease,
KW   inflammation; apoptosis.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
PN   WO9849305-A1.
XX
PD   05-NOV-1998.
XX
PF   29-APR-1998;   98WO-US008631
XX
PR   01-MAY-1997;   97US-0850188
XX
PA   (AMGE-) AMGEN INC.
XX
PI   Boyle WJ,  Wooden S;
XX
DR   WPI; 1999-034661/03.
XX
PT   New chimeric osteoprotegerin polypeptides - contain the
PT   osteoprotegerin dimerisation domain and a heterologous sequence,
PT   useful to treat TNF and TNFR-mediated disorders
XX
PS   Example 1; Fig 4; 92pp; English.
XX
CC   The present invention describes a chimeric polypeptide (A1), comprising
CC   an osteoprotegerin (OPG) dimerisation domain fused to a heterologous
CC   amino acid sequence. Also described are: (1) a multimer polypeptide
CC   comprising covalently associated A1 molecules; (2) an isolated nucleic
CC   acid encoding A1; (3) an expression vector comprising the nucleic acid
CC   sequence; and (4) a host cell transformed or transfected with the
CC   expression vector so that the nucleic acid is expressible. The products
CC   from the present invention are useful to treat a variety of disorders
CC   including those related to receptor binding. Compositions comprising
CC   tumour necrosis factor (TNF), TNFR and TNF receptor (TNFr), e.g. chimeras
CC   are used to treat TNF and TNFR-mediated disorders such as inflammation,
CC   autoimmune diseases and disorders related to excessive apoptosis. The
CC   chimeras are also useful for detecting molecules which interact with
CC   fused heterologous sequences to identify potential new receptors and
CC   ligands. The present sequence represents a TNFbp/OPG construct from
CC   the example of the present invention for creating TNFbp/OPG fusion
CC   proteins.
XX
SQ   Sequence   420 AA;


alignment_scores:
            Quality: 1117.50              Length:    211
              Ratio:  5.588                 Gaps:      1
 Percent Similarity:  94.787   Percent Identity: 94.787

alignment_block:
 US-09-525-998A-11 x AAW89224   ..

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      51 ??????????AA.A?A??????A????...???.............. 87
         ||||||||||||||||||||||||||||||||||||||||||||||||||
      17 uLeuLeuValGlyIleTyrProSerGlyValIleGlyLeuValProHis 34

      88 .....GATAGTGTGTGTCCCCAAGGAAAATATATC 117
                |||||||||||||||||||||||||||||
      34 euGlyAspArgGluLysArgAspSerValCysProGlnGlyLysTyrIle 50

     118 CACCCTCAAAATAATTCGATTGCTGTACCAAGTGCCACAAAGGAACCTA 167
         ||||||||||||||||||||||||||||||||||||||||||||||||||
      51 HisProGlnAsnAsnSerIleCysCysThrLysCysHisLysGlyThrTy 67

     168 CTTGTACAATGACTGTCCAGGCCCGGGGCAGGATACCGACTGCAGGGAGT 217
         ||||||||||||||||||||||||||||||||||||||||||||||||||
      67 rLeuTyrAsnAspCysProGlyProGlyGlnAspThrAspCysArgGluC 84

     218 GTGAGAGCGGCTCCTTCACCGCTTCAGAAAACCACCTCAGACACTGCCTC 267
         ||||||||||||||||||||||||||||||||||||||||||||||||||
      84 ysGluSerGlySerPheThrAlaSerGluAsnHisLeuArgHisCysLeu 100

     268 AGCTGCTCCAAATGCCGAAAGGAAAAGGGTCAGGTGGAGATCTCTTCTTG 317
         ||||||||||||||:||||||||||||||||||||||||||||||||||
     101 SerCysSerLysCysArgLysGluMetGlyGlnValGluIleSerSerCy 117

     318 CACAGTGGACCGGGACACCGTGTGTGGCTGCAGGAAGAACCAGTACCGGC 367
         ||||||||||||||||||||||||||||||||||||||||||||||||||
```

```
     117 sThrValAspArgAspThrValCysGlyCysArgLysAsnGlnTyrArgH 134

     368 ATTATTGGAGTGAAAACCTTTTCCAGTGCTTCAATTGCAGCCTCTGCCTC 417
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     134 isTyrTrpSerGluAsnLeuPheGlnCysPheAsnCysSerLeuCysLeu 150

     418 AATGGGACCGTGCACCTCTCCTGCCAGGAGAAACAGAACACCGTGTGCAC 467
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     151 AsnGlyThrValHisLeuSerCysGlnGluLysGlnAsnThrValCysTh 167

     468 CTGCCATGCAGGTTTCTTTCTAAGAGAAAACGAGTGTGTCTCCTGTAGTA 517
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     167 rCysHisAlaGlyPhePheLeuArgGluAsnGluCysValSerCysSerA 184

     518 ACTGTAAGAAAAGCCTGGAGTGCACGAAGTTGTGCCTACCCCAGATTGAG 567
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     184 snCysLysLysSerLeuGluCysThrLysLeuCysLeuProGlnIleGlu 200

     568 AATGTTAAGGGCACTGAGGACTCAGGCACCACA 600
         ||||||||||||||||||||||||||||||||
     201 AsnValLysGlyThrGluAspSerGlyThrThr 211

seq_name: /SIDS2/gcgdata/geneseq/geneseqp/AA1991.DAT:AAR10986

seq_documentation_block:
ID   AAR10986 standard. Protein. 455 AA.
XX
AC   AAR10986;
XX
DT   13-MAY-1991  (first entry)
XX
DE   30kD TNF inhibitor precursor.
XX
KW   Tumour necrosis factor, inhibitor.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Cleavage-site   40..41
FT                   note=" cleavage gives active protein "
XX
PN   AU9058976-A.
XX
PD   24-JAN-1991.
XX
PF   16-JUL-1990;   90AU-0058976.
XX
PR   07-FEB-1990;   90US-0479661.
PR   18-JUL-1989;   89US-0381080.
PR   11-DEC-1989;   89US-0450329.
XX
PA   (SYNE-) SYNERGEN INC.
XX
DR   WPI; 1991-073847/11.
DR   N-PSDB; AAQ10883.
XX
PT   Tumour necrosis factor inhibitor - for suppression of TNF-alpha
PT   and -beta, useful as therapeutic agent.
XX
PS   Disclosure; Fig 21; 142pp; English
XX
CC   The sequence comprises the entire 30 kD TNF inhibitor. The clone
CC   from which the sequence was deduced was isolated from a cDNA
CC   library prepd. from RNA form U937 cells treated with PMA/PHA.
CC   The whole gene can be inserted into expression vectors for prepn.
CC   of TNF inhibitor for use in the treatment of inflammatory and
CC   degenerative diseases.  The active protein is claimed (Claim 8).
CC   See also AAR10984 and AAR11001.
XX
SQ   Sequence   455 AA;


alignment_scores:

            Quality: 1117.50              Length:    211
              Ratio:  5.588                Gaps:      1
 Percent Similarity:  94.787   Percent Identity: 94.787

alignment_block:
 US-09-525-998A-11 x AAR10986   ..

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      17 uLeuLeuValGlyIleTyrProSerGlyValIleGlyLeuValProHisL 34

      88 ... ..... ... ... .GATAGTGTGTGTCCCCAAGGAAAATATATC 117
                              |||||||||||||||||||||||||||||
      34 euGlyAspArgGluLysArgAspSerValCysProGlnGlyLysTyrIle 50

     118 CACCCTCAAAATAATTGGATTTGCTGTACCAAGTGCCACAAAGGAACCTA 167
         ||||||||||||||||||||||||||||||||||||||||||||||||||
      51 HisProGlnAsnAsnSerIleCysCysThrLysCysHisLysGlyThrTy 67

     168 CTTGTACAATGACTGTCCAGGCCCGGGCAGGATACGGACTGCAGGGAGT 217
         ||||||||||||||||||||||||||||||||||||||||||||||||||
      67 rLeuTyrAsnAspCysProGlyProGlyGlnAspThrAspCysArgGluC 84

     218 GTGAGAGCGGCTCCTTCACGGCTTCAGAAAACCACCTCAGACACTGCCTC 267
         ||||||||||||||||||||||||||||||||||||||||||||||||||
      84 ysGluSerGlySerPheThrAlaSerGluAsnHisLeuArgHisCysLeu 100

     268 AGCTGCTCCAAATGCCGAAAGGAAATGGGTCAGGTGGAGATCTCTTCTTG 317
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     101 SerCysSerLysCysArgLysGluMetGlyGlnValGluIleSerSerCy 117

     318 CACAGTGCACCGGGACACCGTGTGTGGCTGCAGGAAGAACCAGTACCGGC 367
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     117 sThrValAspArgAspThrValCysGlyCysArgLysAsnGlnTyrArgH 134

     368 ATTATTGGAGTGAAAACCTTTTCCAGTGCTTCAATTGCAGCCTCTGCCTC 417
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     134 isTyrTrpSerGluAsnLeuPheGlnCysPheAsnCysSerLeuCysLeu 150

     418 AATGGGACCGTGCACCTCTCCTGCCAGGAGAAACAGAACACCGTGTGCAC 467
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     151 AsnGlyThrValHisLeuSerCysGlnGluLysGlnAsnThrValCysTh 167

     468 CTGCCATGCAGGTTTCTTTCTAAGAGAAAACGAGTGTGTCTCCTGTAGTA 517
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     167 rCysHisAlaGlyPhePheLeuArgGluAsnGluCysValSerCysSerA 184

     518 ACTGTAAGAAAAGCCTGGAGTGCACGAAGTTGTGCCTACCCCAGATTGAG 567
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     184 snCysLysLysSerLeuGluCysThrLysLeuCysLeuProGlnIleGlu 200

     568 AATGTTAAGGGCACTGAGGACTCAGGCACCACA 600
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     201 AsnValLysGlyThrGluAspSerGlyThrThr 211

seq_name: /SIDS2/gcgdata/geneseq/geneseqp/AA1991.DAT:AAR11082

seq_documentation_block:
ID   AAR11082 standard; Protein; 455 AA.
XX
AC   AAR11082;
XX
DT   24-MAY-1991  (first entry)
XX
DE   Human 55kD TNF-binding protein.
XX
KW   Tumour Necrosis Factor; binding proteins; septic shock;
```

```
KW   autoimmune glomerulonephritis; lymphokine; cytokine.
XX
FH   Key             Location/Qualifiers
FT   Modified-site   54
FT                   /label= putative N-glycosylation site
FT   Modified-site   145
FT                   /label= putative N-glycosylation site
FT   Modified-site   151
FT                   /label= putative N-glycosylation site
FT   Modified-site   270
FT                   /label= putative N-glycosylation site
FT   Region          212..230
FT                   /label= transmembrane region
FT   Peptide         1..28
FT                   /label= signal peptide
XX
PN   EP417563-A.
XX
PD   20-MAR-1991.
XX
PF   31-AUG-1990;    90EP-0116707.
XX
PR   20-APR-1990;    90CH-0001347.
PR   12-SEP-1989;    89CH-0033319.
PR   08-MAR-1990;    90CH-0000746.
XX
PA   (HOFF ) HOFFMANN-LA ROCHE AG.
XX
PI   Brockhaus M,  Dembic Z,  Gentz R,  Lesslauer W,  Lotscher H;
PI   Schlaeger EJ;
XX
DR   WPI; 1991-081851/12.
DR   N-PSDB; AAQ10955.
XX
PT   Insoluble tumour necrosis factor binding proteins - and DNA
PT   encoding them, useful in pharmaceutical prods. and for antibody
PT   prodn.
XX
PS   Claim 1; Fig 1; 26pp; German.
XX
CC   Partial amino acid sequences were determined for the 55 and 75kD
CC   TNF-BPs (see AAR11072-R11081) and oligonucleotide primers were
CC   synthesised based on these partial sequences. The primers were used
CC   to produce a cDNA fragment for use as a probe to screen a human
CC   placental cDNA bank constructed in lambda gt11. Positive clones were
CC   identifed and sequenced. DNA constructs comprising the TNF-BP coding
CC   sequence may also contain a fragment encoding a human Ig domain.
CC   Recombinant constructs are used to transform cells to confer
CC   improved TNF-binding properties.
CC   See also AAQ10956.
XX
SQ   Sequence   455 AA;


alignment_scores:
            Quality: 1117.50              Length:    211
              Ratio:  5.588                 Gaps:      1
 Percent Similarity:  94.787   Percent Identity: 94.787

alignment_block:
 US-09-525-998A-11 x AAR11082   ..

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      51 GCTGTTGGTGGGAATATACCCCTCAGGGGTTATTGGA      . . . .  87
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      17 uLeuLeuValGlyIleTyrProSerGlyValIleGlyLeuValProHisL 34

      88 ....................GATAGTGTGTGTCCCCAAGGAAAATATATC 117
                                 ||||||||||||||||||||||||||||
      34 euGlyAspArgGluLysArgAspSerValCysProGlnGlyLysTyrIle 50

     118 CACCCTCAAAATAATTCGATTTGCTGTACCAACTGCCACAAAGGAACCTA 167
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      51 HisProGlnAsnAsnSerIleCysCysThrLysCysHisLysGlyThrTy 67

     168 CTTGTACAATGACTGTCCAGGCCCGGGGCAGGATACGGACTGCAGGGAGT 217
         |||||||||||||||||||||||||||||||||||||||||||||||||
      67 rLeuTyrAsnAspCysProGlyProGlyGlnAspThrAspCysArgGluC 84

     218 GTGAGAGCGGCTCCTTCACCGCTTCAGAAAACCACCTCAGACACTGCCTC 267
         |||||||||||||||||||||||||||||||||||||||||||||||||
      84 ysGluSerGlySerPheThrAlaSerGluAsnHisLeuArgHisCysLeu 100
                                                .
     268 AGCTGCTCCAAATGCCGAAAGGAAATCGGTCAGGTGGAGATCTCTTCTTG 317
         |||||||||||||||||||||||||||||||||||||||||||||||||
     101 SerCysSerLysCysArgLysGluMetGlyGlnValGluIleSerSerCy 117

     318 CACAGTGGACCGGGACACCGTGTGTGGCTGCAGGAAGAACCAGTACCGGC 367
         |||||||||||||||||||||||||||||||||||||||||||||||||
     117 sThrValAspArgAspThrValCysGlyCysArgLysAsnGlnTyrArgH 134

     368 ATTATTGGAGTGAAAACCTTTTCCAGTGCTTCAATTGCAGACTCTGCCTC 417
         |||||||||||||||||||||||||||||||||||||||||||||||||
     134 isTyrTrpSerGluAsnLeuPheGlnCysPheAsnCysSerLeuCysLeu 150

     418 AATGGGACCGTGCACCTCTCCTGCCAGGAGAAACAGAACACCGTGTGCAC 467
         |||||||||||||||||||||||||||||||||||||||||||||||||
     151 AsnGlyThrValHisLeuSerCysGlnGluLysGlnAsnThrValCysTh 167

     468 CTGCCATGCAGGTTTCTTCTCTAAGAGAAAACGAGTGTGTCTCCCTGTAGTA 517
         |||||||||||||||||||||||||||||||||||||||||||||||||
     167 rCysHisAlaGlyPhePheLeuArgGluAsnGluCysValSerCysSerA 184

     518 ACTGTAAGAAAAGCCTGGAGTGCACGAAGTTGTGCCTACCCCAGATTGAG 567
         |||||||||||||||||||||||||||||||||||||||||||||||||
     184 snCysLysLysSerLeuGluCysThrLysLeuCysLeuProGlnIleGlu 200

     568 AATGTTAAGGGCACTGAGGACTCAGGCACCACA 600
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     201 AsnValLysGlyThrGluAspSerGlyThrThr 211

seq_number:  [illegible]

seq_documentation_block:
ID   AAR20787 standard; Protein; 455 AA.
XX
AC   AAR20787;
XX
DT   11-MAY-1992  (first entry)
XX
DE   TNF-alpha binding protein.
XX
KW   Tumour necrosis factor alpha; autoimmune diseases; cachectin;
KW   extracellular domain.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..40
FT                   /note= "signal peptide"
FT   Peptide         41..455
FT                   /note= "mature peptide"
FT   Domain          30..199
FT                   /note= "extracellular domain"
FT   Domain          212..234
FT                   /note= "transmembrane domain"
FT   Modified site   145..147
FT                   /note= "potential N-glycosylation site"
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FT                   /note= "potential N-glycosylation site"
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PN   GB2246569-A.
XX
PD   05-FEB-1992.
XX
PF   15-JUN-1990;   90GB-0013410.
XX
PR   15-JUN-1990;   90GB-0013410.
XX
PA   (CHAR-) CHARING CROSS SUNLE.
XX
PI   Feldman M,  Gray P,  Turner M,  Brennan F;
XX
DR   WPI; 1992-043613/06.
DR   N-PSDB; AAQ20973.
XX
PT   New tumour necrosis factor alpha binding protein and polypeptide
PT   - useful in treating cachexia, sepsis and auto immune diseases
PT   e.g. rheumatoid arthritis
XX
PS   Disclosure; Fig 1; 25pp, English
XX
CC   The amino acid sequence is that of tumour necrosis factor alpha
CC   binding protein which contains the extracellular domain of human TNF
CC   alpha receptor. It is soluble and can be used in the regulation of
CC   TNF-mediated responses by binding and sequestering the cytokine. It
CC   can therefore be used therapeutically to treat disorders such as
CC   cachexia, sepsis and autoimmune diseases, specifically rheumatoid
CC   arthritis.
XX
SQ   Sequence   455 AA;


alignment_scores:
            Quality. 1117.50              Length:    211
              Ratio.  5.588                Gaps:      1
 Percent Similarity:  94.787   Percent Identity: 94.787

alignment_block:
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      51 GCTGTTGGTGGGAATATACCCCTCAGGGGTTATTGGA...  .  .  .  . 87
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      17 uLeuLeuValGlyIleTyrProSerGlyValIleGlyLeuValProHisL 34

      88                  GATAGTGTGTGTCCCCAAGGAAAATATATC 117
                          |||||||||||||||||||||||||||||
      34 euGlyAspArgGluArgLysAspSerValCysProGlnGlyLysTyrIle 50

     118 CACCCTCAAAATAATTCGATTTGCTGTACCAAGTGCCACAAAGGAACCTA 167
         ||||||||||||||||||||||||||||||||||||||||||||||||||
      51 HisProGlnAsnAsnSerIleCysCysThrLysCysHisLysGlyThrTy 67

     168 CTTGTACAATGACTGTCCAGGCCCGGGGCAGGATACGGACTGCAGGAGT 217
         ||||||||||||||||||||||||||||||||||||||||||||||||||
      67 rLeuTyrAsnAspCysProGlyProGlyGlnAspThrAspCysArgGluC 84

     218 CTGAGACCCGCTCCTTCACCGCTTCAGAAAACCACCTCAGACACTGCCTC 267
         ||||||||||||||||||||||||||||||||||||||||||||||||||
      84 ysGluSerGlySerPheThrAlaSerGluAsnHisLeuArgHisCysLeu 100

     268 AGTTGCTCCAAAIGCCGAAAGGAAATGGGTCAGGTGGAGATCTCTTCTTG 317
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     101 SerCysSerLysCysArgLysGluMetGlyGlnValGluIleSerSerCy 117

     318 CACAGTGGACCGGGACACCGTGTGTGGCTGCAGGAAGAACCAGTACCGGC 367
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     117 sThrValAspArgAspThrValCysGlyCysArgLysAsnGlnTyrArgH 134

     368 ATTATTGGAGTGAAAACCTTTTCCAGTGTTCAATTGCAGCTCTGCCTC 417
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     134 isTyrTrpSerGluAsnLeuPheGlnCysPheAsnCysSerLeuCysLeu 150

     418 AATGGGACCGTGCACCTCTCCTGCCAGGAGAAACAGAACACCGTGTGCAC 467
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     151 AsnGlyThrValHisLeuSerCysGlnGluLysGlnAsnThrValCysTh 167

     468 CTGCCATGCAGGTTTCTTTCTAAGAGAAAACGAGTGTGTCTCCTGTAGTA 517
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     167 rCysHisAlaGlyPhePheLeuArgGluAsnGluCysValSerCysSerA 184

     518 ACTGTAAGAAAAGCCTGGAGTGCAAGAAGTTGTGCCTACCCCAGATTGAG 567
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     184 snCysLysLysSerLeuGluCysThrLysLeuCysLeuProGlnIleGlu 200

     568 AATGTTAAGGGCACTGAGGACTCAGGCACCACA 600
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     201 AsnValLysGlyThrGluAspSerGlyThrThr 211

seq_name: /SIDS2/gcgdata/geneseq/geneseqp/AA1992.DAT:AAR24000

seq_documentation_block:
ID   AAR24000 standard; Protein; 455 AA.
XX
AC   AAR24000;
XX
DT   05-NOV-1992  (first entry)
XX
DE   TNF-alpha 55kD receptor.
XX
KW   tumour necrosis factor alpha; extracellular binding domain;
KW   treatment, pulmonary diseases; septic shock; HIV infection; AIDS;
KW   malaria; viral meningits; graft versus host disease;
KW   autoimmune disease; rheumatoid arthritis.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..40
FT                   /label= signal peptide
FT   Modified-site   54..56
FT                   /label= N linked glycosylation site
FT                   /note= "potential"
FT   Modified-site   145..147
FT                   /label= N linked glycosylation site
FT                   /note= "potential "
FT   Modified-site   151..153
FT                   /label= N linked glycosylation site
FT                   /note= "potential"
FT   Domain          212..234
FT                   /label= transmembrane domain
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PN   WO9207076-A.
XX
PD   30-APR-1992.
XX
PF   18-OCT-1991;   91WO-GB01826.
XX
PP   18-OCT-1990;   90GB-0022648
XX
PA   (CHAR-) CHARING CROSS SUNLEY RES CENT.
XX
PI   Brennan FM,  Feldmann M,  Gray PW,  Turner MJC;
XX
DR   WPI; 1992-167156/20
DR   N-PSDB; AAQ24440.
XX
PT   New polypeptide capable of binding human TNF alpha - comprises
PT   first three cysteine-rich subdomains of TNF alpha receptor for
PT   treating autoimmune disease, septic shock, HIV etc.
XX
```

```
PS   Example; Fig 1; 43pp; English.
XX
CC   This sequence was deduced from human TNF-alpha cDNA isolated as in
CC   AAQ24440. The first 35 amino acids are generally quite hydrophobic
CC   and probably represent a signal sequence. Residues 35-40  are highly
CC   charged (DREKR) and this is not normally found in secretory
CC   signal sequences. It is possible the receptor is processed by
CC   proteolysis after residue 40 which contains a dibasic cleavage site
CC   (KR). Hydropathy analysis of this sequence predicts a single
CC   transmembrane domain of 23 amino acids, dividing the sequence into
CC   an extracellular domain of 171 residues and a cytoplasmic domain of
CC   221 residues. The sequence contains a large number of cysteine
CC   residues, the arrangement of which is similar to that of other cell
CC   surface proteins, suggesting the TNF-alpha receptor is structurally
CC   related to a family of receptors.
CC   NOTE:- Residues 371,2 given in the sequence as T,L, are encoded by
CC   TGG (W) and AAG (K).
CC   See also AAQ24440-51, AAR24000, AAR24080-84, AAR27585, AAQ29236-8
XX
SQ   Sequence   455 AA;


alignment_scores:
            Quality: 1117.50            Length:    211
              Ratio:  5.588              Gaps:      1
 Percent Similarity:  94.787   Percent Identity: 94.787

alignment_block:
 US-09-525-998A-11 x AAR24000   ..

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       1 MetGlyLeuSerThrValProAspLeuLeuLeuProLeuValLeuLeuGl 17

      51 GCTGTTGGTGGGAATATACCCCTCAGGGGTTATTGGA..............  87
         |||||||||||||||||||||||||||||||||||
      17 uLeuLeuValGlyIleTyrProSerGlyValIleGlyLeuValProHisL  34

      88                      GAIAGTGTGTGTCCCCAAGGAAAATATATC 117
                              |||||||||||||||||||||||||||||
      34 euGlyAspArgGluLysArgAspSerValCysProGlnGlyLysTyrIle 50

     118 CACCCTCAAAATAATTCGATTTGCTGTACCAAGTGCCACAAAGGAACCTA 167
         |||||||||||||||||||||||||||||||||||||||||||||||||||
      51 HisProGlnAsnAsnSerIleCysCysThrLysCysHisLysGlyThrTy 67

     168 CTTGTACAATGACTGTGCCAGGCCGGGGGCAGGATACGGACTGCAGGGAGT 217
         |||||||||||||||||||||||||||||||||||||||||||||||||||
      67 rLeuTyrAsnAspCysProGlyProGlyGlnAspThrAspCysArgGluC 84

     218 GTGAGAGCGGCTCTTTCACCGCTCAGAAAACCACCTCAGACACTGCCTC 267
         |||||||||||||||||||||||||||||||||||||||||||||||||||
      84 ysGluSerGlySerPheThrAlaSerGluAsnHisLeuArgHisCysLeu 100

     268 AGCTGCTCCAAATGCCGAAAGGAAATGGGTCAGGTGGAGATCTCTTCTTG 317
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     101 SerCysSerLysCysArgLysGluMetGlyGlnValGluIleSerSerCy 117

     318 CACAGTGGACGGGGACAGCCGTGTGTGCCTGCAGGAAGAACCAGTACCGGC 367
         |||||||||||||||||||||||||||||||||||||||||||||||||||
     117 sThrValAspArgAspThrValCysGlyCysArgLysAsnGlnTyrArgH 134

     368 ATTATTGGAGTGAAAACCTTTTCCAGTGCTTCAATTGCAGCCCTCTGCCTC 417
         |||||||||||||||||||||||||||||||||||||||||||||||||||
     134 isTyrTrpSerGluAsnLeuPheGlnCysPheAsnCysSerLeuCysLeu 150

     418 AATGGGACCGTGCACCTCTCCTGCCAGGAGAAACAGAACACCGTGTGCAC 467
         |||||||||||||||||||||||||||||||||||||||||||||||||||
     151 AsnGlyThrValHisLeuSerCysGlnGluLysGlnAsnThrValCysTh 167

     468 CTGCCATGCAGGTTTCTTTCTAAGAGAAAACGAGTGTGTCTCCTGTAGTA 517
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         |||||||||||||||||||||||||||||||||||||||||||||||||||
     167 rCysHisAlaGlyPhePheLeuArgGluAsnGluCysValSerCysSerA 184

     518 ACTGTAAGAAAAGCCGGGAGTGCACGAAGTGTGCGCCAGCCCAGATTGAG 567
         |||||||||||||||||||||||||||||||||||||||||||||||||||
     184 snCysLysLysSerLeuGluCysThrLysLeuCysLeuProGlnIleGlu 200

     568 AATGTTAAGGGCACTGAGGACTCAGGCACCACA 600
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     201 AsnValLysGlyThrGluAspSerGlyThrThr 211

Seq_summary_SIDS_1 1117.5, 211 seq, 0 rev seq, between AA.*.*:AAI:AAR42059

seq_documentation_block:
ID   AAR42059 standard; Protein; 455 AA.
XX
AC   AAR42059;
XX
DT   29-APR-1994  (first entry)
XX
DE   Lambda derived TNF-R.
XX
KW   Human; tumour necrosis factor receptor; TNF-R; interleukin-1 receptor;
KW   IL-1R, fusion protein, linker, TNF, IL-1, cachexia, cerebral malaria;
KW   rheumatoid arthritis; diabetes, multiple sclerosis, septic shock;
KW   pulmonary fibrosis, silicosis, allograft, armograft, rejection;
KW   graft verses host disease; sepsis; inflammation; allergy;
KW   autoimmune dysfunction.
XX
OS   Homo sapiens.
OS   Lambda-gt10 ?cDNAlbp.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..40
FT                   /note= "Signal peptide"
FT   Protein         41..455
FT                   /note= "Mature hTNF-R"
XX
PN   WO9313777-A.
XX
PD   14-OCT-1993.
XX
PF   26-MAR-1993;   93WO-US02938.
XX
PR   30-MAR-1992;   92US-0860710.
XX
PA   (IMMV ) IMMUNEX CORP.
XX
PI   Smith CA;
XX
DR   WPI; 1993-326962/41.
DR   N-PSDB; AAQ49942.
XX
PT   New fusion protein tumour necrosis factor and human interleukin-1
PT   receptor - useful in therapy, diagnosis and assays of e.g.
PT   rheumatoid arthritis, diabetes, cerebral malaria, sepsis, etc.
XX
PS   Disclosure; Page 57-59; 85pp; English.
XX
CC   The sequences given in AAR42058-59 represent human tumour necrosis
CC   factor receptor (TNF-R) and the sequences in AAR42060-61 represent
CC   human interleukin 1 receptor (IL-1R).  These sequences were used in
CC   the production of a fusion protein which conformed to one of the
CC   formulae:
CC        TNF-R-linker-TNF-R-linker-IL-1R
CC        IL-1R-linker-TNF-R-linker-TNF-R or
CC        TNF-R-linker-TNF-R
CC   The linker may comprise 5-100 amino acids selected from Gly, Asp,
CC   Ser, Thr and Ala.  These linkers separate the individual moeities
CC   by such a distance that each component of the fusion protien is
CC   capable of folding into the secondary or tertiary structure required
CC   for its biological activity.  These fusion proteins may be used in
CC   therapy, diagnosis and assays for conditions mediated by TNF or IL-1,
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CC   particularly in conditions in which both TNF and IL-1 play a causitive
CC   role.  They may be used to treat cachexia, rheumatoid arthritis,
CC   diabetes, multiple sclerosis, pulmonary fibrosis and silicosis,
CC   cerebral malaria, allograft and xenograft rejection in graft verses
CC   host disease, sepsis, septic shock, inflammation, allergies and
CC   autoimmune dysfunctions.
XX
SQ   Sequence   455 AA;


alignment_scores:
            Quality: 1117.50              Length:    211
              Ratio:  5.588                Gaps:      1
 Percent Similarity:  94.787   Percent Identity: 94.787

alignment_block:
 US-09-525-998A-11 x AAR42059   ..

 Align seq 1/1  to: AAR42059  from: 1  to: 455

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      51 GCTGTTGGTGGGAATATACCCCTCAGGGGTTATTGGA.. ..... 87
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      17 uLeuLeuValGlyIleTyrProSerGlyValIleGlyLeuValProHisL 34

      88  ..... GATAGTGTGTGTCCCCAAGGAAAATATATC 117
                ||||||||||||||||||||||||||||||
      34 euGlyAspArgGluLysArgAspSerValCysProGlnGlyLysTyrIle 50

     118 CACCCTCAAAATAATTCGATTTGCTGTACCAAGTGCCACAAAGGAACCTA 167
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     168 CTTGTACAATGACTGTGCAGGCCGGGGCAGGATACTGCACGGGAGT 217
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      67 rLeuTyrAsnAspCysProGlyProGlyGlnAspThrAspCysArgGluC 84

     218 GTGAGAGCCCCTCCTTCACCGCTTCAGAAAACCACCTCAGACACTGCCTC 267
         |||||||||||||||||||||||||||||||||||||||||||||||||||
      84 ysGluSerGlySerPheThrAlaSerGluAsnHisLeuArgHisCysLeu 100

     268 AGCTGCTCCAAATGCCGAAAGGAAATGGGTCAGGTGGAGATCTCTTCTTC 317
         |||||||||||||||||||||||||||||||||||||||||||||||||||
     101 SerCysSerLysCysArgLysGluMetGlyGlnValGluIleSerSerCy 117

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     117 sThrValAspArgAspThrValCysGlyCysArgLysAsnGlnTyrArgH 134

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     418 AATGGGACCGTGCACCTCTCCTGCCAGGAGAAACAGAACACCGTGTGCAC 467
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     151 AsnGlyThrValHisLeuSerCysGlnGluLysGlnAsnThrValCysTh 167

     468 CTGCCATGCAGGTTTCTTTCTAAGAGAAAACGAGTGTGTCTCCTGTAGTA 517
         |||||||||||||||||||||||||||||||||||||||||||||||||||
     167 rCysHisAlaGlyPhePheLeuArgGluAsnGluCysValSerCysSerA 184

     518 ACTGTAAGAAAAGCCTGGAGTCCACGAAGTTGTGCCTACCCCAGATTCAC 567
         |||||||||||||||||||||||||||||||||||||||||||||||||||
     184 snCysLysLysSerLeuGluSerThrLysLeuCysLeuProGlnIleGlu 200

     568 AATGTTAAGGGCACTGAGGACTCAGGCACCACA 600
         |||||||||||||||||||||||||||||||
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seq_name: /SIDS2/gcgdata/geneseq/geneseqp/AA1995.DAT:AAR75084
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seq_documentation_block:
ID   AAR75084 standard; Protein; 455 AA.
XX
AC   AAR75084;
XX
DT   19-JAN-1996  (first entry)
XX
DE   p55 TNF-R.
XX
KW   p55; tumour necrosis factor receptor; TNF-R; human; murine; chimera;
KW   epidermal growth factor receptor; EGF-R; protease; inhibitor;
KW   phorbol myristate acetate; PMA.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Peptide         41..53
FT                   /note= "N terminus of soluble p55 TNF-R"
FT   Modified-site   54..56
FT                   /note= "glycosylation site"
FT   Modified-site   145..147
FT                   /note= "glycosylation site"
FT   Modified-site   161..163
FT                   /note= "glycosylation site"
FT   Peptide         193..210
FT                   /note= "peptide used in creation of chimeras"
FT   Region          198..210
FT                   /note= "spacer region"
FT   Misc-difference 201
FT                   /note= "major C terminus for soluble p55 TNF-R"
FT   Misc-difference 202
FT                   /note= "essential for shedding reaction"
FT   Misc-difference 203
FT                   /note= "minor C terminus for soluble p55 TNF-R"
FT   Region          212..234
FT                   /note= "transmembrane region"
XX
PN   AU9475742-A.
XX
PD   04-MAY-1995.
XX
PF   11-OCT-1994;   94AU-0075742.
XX
PR   12-OCT-1993;   9311L 0107268.
XX
PA   (YEDA ) YEDA RES & DEV CO LTD.
XX
PI   Batkin M,  Brakebusch C,  Varfolomeev E,  Wallach D;
XX
DR   WPI, 1995 194342/26.
DR   N-PSDB; AAQ90513.
XX
PT   New protease capable of cleaving soluble tumour necrosis factor
PT   (TNF) receptor  - from cell-bound TNF- receptor, useful for
PT   antagonising deleterious effects of TNF.
XX
PS   Disclosure; Fig 1; 40pp; English.
XX
CC   This sequence represents human p55 tumour necrosis factor (TNF-R).
CC   Expression of this receptor is regulated by shedding of the
CC   extracellular receptor fragment.  The p55 TNF-R can be shed in response
CC   to different inducing agents, e.g. phorbol myristate acetate (PMA),
CC   depending on cell type.  The only region of the receptor whose structure
CC   affects the shedding response is the spacer region (see AAR75012) in the
CC   extracellular domain.  This region is located close to a site of cleavage
CC   of the molecule, and links the Cys rich module to the transmembrane
CC   domain.  The spacer region of the encoded protein was used to create the
CC   chimeras between human p55 TNF-R and murine epidermal growth factor
CC   receptor (EGF-R) that are represented by AAR75007-11.  This spacer region
CC   was subjected to deletion mutations (AAR75013-25) and substitutions
CC   (AAR75026-47).  Of the spacer region, the most important residues are
CC   Asn 172, Val 173, Lys 174 and Gly 175, with Val 173 being the most
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CC   important of these.  The shedding of the receptor is independent of the
CC   side chain identity of these residues, with the exception of a limited
CC   dependence on the identity of Val 173.  Mutations which alter the
CC   conformation of the protein adversely effect the shedding process.
CC   The mutations shown in AAR75013-47 were introduced in order to create an
CC   inhibitor of a protease that is capable of cleaving the soluble TNF-R
CC   from the cell bound TNF-R.  Fragments of these inhibitors can be seen in
CC   AAR75017-9, AAR75025, AAR75033-5 and AAR75042-3.  These protease
CC   inhibitors can be used for enhancing TNF function.
XX
SQ   Sequence   455 AA;


alignment_scores:
            Quality: 1117.50              Length:    211
              Ratio:  5.588                Gaps:      1
 Percent Similarity:  94.787   Percent Identity: 94.787

alignment_block:
 US-09-525-998A-11 x AAR75084   ..

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         |||||||||||||||||||||||||||||||||||
      17 uLeuLeuValGlyIleTyrProSerGlyValIleGlyLeuValProHisL 34

      88 .....GATACTGTGTGTCCCCAAGGAAAATATATC 117
                ||||||||||||||||||||||||||||||
      34 euGlyAspArgGluLysArgAspSerValCysProGlnGlyLysTyrIle 50

     118 CACCCTCAAAATAATTCGATTTGCTGTACCAACTGCCACAAAGCAACCTA 167
         |||||||||||||||||||||||||||||||||||||||||||||||||
      51 HisProGlnAsnAsnSerIleCysCysThrLysCysHisLysGlyThrTy 67

     168 CTTGTACAATGACTGTCCAGGCCCGGGGCAGGATACGGACTGCAGGGAGT 217
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      67 rLeuTyrAsnAspCysProGlyProGlyGlnAspThrAspCysArgGluC 84

     218 GTGAGAGCGGCTCCTTCACCGCTTCAGAAAACCACCTCACACACTGCCTC 267
         |||||||||||||||||||||||||||||||||||||||||||||||||
      84 ysGluSerGlySerPheThrAlaSerGluAsnHisLeuArgHisCysLeu 100

     268 AGCTGCTCCAAATGCCGAAAGGAAATGGGTCAGGTGGAGATCTCTTCTTG 317
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     418 AATGGGACCGTGCACCTCTCCTGCCAGGAGAAACAGAACACCGTGTGCAC 467
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     151 AsnGlyThrValHisLeuSerCysGlnGluLysGlnAsnThrValCysTh 167

     468 CTGCCATGCAGGTTTCTTTCTAAGAGAAAACGAGTGTGTCTCCTGTAGTA 517
         |||||||||||||||||||||||||||||||||||||||||||||||||
     167 rCysHisAlaGlyPhePheLeuArgGluAsnGluCysValSerCysSerA 184

     518 ACTCTAACAAAAGCCTGGAGTGCCACCAAGTGTGGCCTACCCCAGATTGAG 567
         |||||||||||||||||||||||||||||||||||||||||||||||||
     184 snCysLysLysSerLeuGluCysThrLysLeuCysLeuProGlnIleGlu 200

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seq_documentation_block:
ID   AAY30934 standard; Protein; 455 AA.
XX
AC   AAY30934;
XX
DT   18-OCT-1999  (first entry)
XX
DE   Human tumour necrosis factor binding protein.
XX
KW   Tumour necrosis factor binding protein; TNF; insoluble protein; agonist;
KW   anti-inflammatory; antimalarial; treatment; septic shock; inflammation;
KW   autoimmune glomerulonephritis; cerebral malaria; immune response;
KW   antagonist; diagnosis.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..29
FT                   /label= signal_peptide
FT   Protein         30..455
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FT                   /note= "hypothetical glycosylation site"
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PN   EP939121-A2.
XX
PD   01-SEP-1999.
XX
PF   31-AUG-1998;   98EP-0116787.
XX
PR   26-APR-1996;   96CH-0001347.
PR   12-SEP-1989;   89CH-0003319.
PR   08-MAR-1990;   90CH-0000746.
XX
PA   (HOFF ) HOFFMANN LA ROCHE & CO AG F.
XX
PI   Brockhaus M;  Dembic Z;  Gentz R;  Lesslauer W;  Loetscher H;
PI   Schlaeger E;
XX
DR   WPI; 1999-480840/41.
DR   N-PSDB; AAZ09170.
XX
PT   New insoluble proteins, and fragments, that bind to tumor necrosis
PT   factor, used to treat e.g. septic shock or cerebral malaria
XX
PS   Claim 4a; Fig 1; 25pp; German.
XX
CC   This invention describes novel homogeneous insoluble proteins (I),
CC   their (in)soluble fragments (Ia) and their salts that can bind tumour
CC   necrosis factor (TNF), the products of the invention have
CC   anti inflammatory and antimalarial activity. (I) and (Ia) are used (i)
CC   to treat diseases in which TNF is involved (e.g. septic shock, autoimmune
CC   glomerulonephritis, cerebral malaria, immune responses and inflammation),
CC   (ii) to purify TNF, (iii) to identify TNF (ant)agonists and (iv) for
CC   diagnostic determination of TNF in body fluids. Antibodies raised against
CC   (I) are used for affinity purification of (i). This sequence represents
CC   a tumour necrosis factor binding protein described in the method of
CC   the invention.
XX
SQ   Sequence   455 AA;
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alignment_scores:
            Quality: 1117.50              Length:    211
              Ratio:  5.588                Gaps:        1
 Percent Similarity:  94.787   Percent Identity: 94.787

alignment_block:
 US-09-525-998A-11 x AAY30934   ..

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      51 GCTGTTGGTGGGAATATACCCCTCAGGGGTTATTGGA..............  87
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      17 uLeuLeuValGlyIleTyrProSerGlyValIleGlyLeuValProHisL 34

      88 ....................GATAGTGTGTGTCCCCAAGGAAAATATATC 117
                             |||||||||||||||||||||||||||||
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     118 CACCCTCAAAATAATTCGATTTGCTGTACCAAGTGCCACAAAGGAACCTA 167
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     168 CTTGTACAATGACTGTCCAGGCCCGGGGCAGGATACGGACTGCAGGGAGT 217
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      67 rLeuTyrAsnAspCysProGlyProGlyGlnAspThrAspCysArgGluC 84

     218 GTGAGAGCGGCTCCTTCACCGCTTCAGAAAACCAGCTCAGACACTGCCTC 267
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      84 ysGluSerGlySerPheThrAlaSerGluAsnHisLeuArgHisCysLeu 100

     268 AGCTGCTCCAAAIGCCGAAAGGAAATGGGTCAGGTGGAGATCTCTTCTTG 317
         |||||||||||||||||||||||||||||||||||||||||||||||||||
     101 SerCysSerLysCysArgLysGluMetGlyGlnValGluIleSerSerCy 117

     318 CACAGTGCACGGGACACCGTGTGTGGCTGCAGGAAGAACCAGTACCGGC 367
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     117 sThrValAspArgAspThrValCysGlyCysArgLysAsnGlnTyrArgH 134

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         |||||||||||||||||||||||||||||||||||||||||||||||||||
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     418 AATGGGACCGTGCACCTCTCCTGCCAGGAGAAACAGAACACCGTGTGCAC 467
         |||||||||||||||||||||||||||||||||||||||||||||||||||
     151 AsnGlyThrValHisLeuSerCysGlnGluLysGlnAsnThrValCysTh 167

     468 CTGCCATGCAGGTTTCTTTCTAAGAGAAAACGAGTGTGTCTCCTGTAGTA 517
         |||||||||||||||||||||||||||||||||||||||||||||||||||
     167 rCysHisAlaGlyPhePheLeuArgGluAsnGluCysValSerCysSerA 184

     518 ACTGTAAGAAAAGCCTGGAGTGCACGAAGTTGTGCCTACCCCAGATTGAG 567
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